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09/771,382	01/25/2001	Ian Richard Anselm Peak	8795-24 U1	6450

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EXAMINER	
FORD, VANESSA L	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/771,382	PEAK ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133) Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34 and 49-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *33,34 and 49-52* is/are allowed.

6)☒ Claim(s) *53-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to Applicant's amendment and response filed June 8, 2007. Claims 53 and 56 have been amended. Claims 1-32, and 35-48 have been cancelled. Claims 33-34 and 49-58 are under examination.

Rejection Withdrawn

2. In view of Applicant's amendment and response, the rejection under 35 U.S.C. 112 second paragraph, pages 13, paragraph 7 of the previous Office action is withdrawn

Rejections Maintained

3. The rejection under 35 U.S.C. 112, first paragraph (enablement) is maintained for 53-58 for the reasons set forth on pages 3-9, paragraph 4 of the Final Office Action. The rejection is reiterated below:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The claims 53-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated proteins as set forth in SEQ ID NOs: 23 and 35 and compositions comprising the isolated proteins, does not reasonably provide enablement for proteins that are variants of SEQ ID NOs: 23 or 35 or compositions comprising these proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification broadly discloses a genus of polypeptides that comprises SEQ ID NO:23 and SEQ ID NO:35. The instant specification teaches that SEQ ID NO: 23 is the amino acid sequence of a PMC 21 NhhA deletion mutant polypeptide (page 8 and Example 4). The instant specification teaches that SEQ ID NO: 35 is the amino acid sequence of a predicted mature protein described in Example

4 (page 10 and Example 4). The instant specification teaches that recombinant DNA-based production of the polypeptides of the invention can be accomplished by the deletion of one or a few amino acids of the (conserved) C1, C2, C3, C4 and/or C5 or (variable) V1, V2, V3 and/or V4 regions of the consensus polypeptide (SEQ ID NO:11) (page 13). The specification teaches that SEQ ID NO:11 comprises constant regions of NhhA polypeptide designated as C1-C5 and non-conserved regions designated as V1-V-4 (page 3). The instant specification teaches that V1-V4 are non-conserved amino acids of a variable region (page 3). Therefore, the non-conserved regions of SEQ ID NO:11 can comprise any amino acid. Thus, the claimed polypeptide as set forth in SEQ ID NO:11 as well as variants of SEQ ID NOs. 23 and 35 can include any substitution or change of amino acids throughout regions V1-V4 of the polypeptide sequence. Therefore, SEQ ID No: 11 and variant or fragments of SEQ ID NOs: 23 and 35 can correspond to mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth are being claimed. There is no guidance provided as to which amino acids can be substituted, inserted or deleted and the polypeptide would retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity/utility requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation. There is no guidance as to what amino acids may not be changed without causing a detrimental effect to the polypeptide being claimed. The claims broadly teach polypeptides, which include substitutions and/or deletions, therefore any polypeptide is being claimed, and no specific location for the deletion, substitution or any combination thereof is recited. Thus, the resulting polypeptide could result in a polypeptide not taught nor enabled by the specification.

The claims of the instant application are not only drawn to isolated proteins but are also drawn to isolated proteins that have at least 80% or at least 90% identity to SEQ ID NOs. 23 and 35. Thus, the claimed isolated proteins include variants as well as fragments of SEQ ID NOs 23 and 35. There is no guidance provided in the specification as how one would begin to choose " variants or fragments" of SEQ ID NOs: 23 or 35. The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does not disclose the following:

- the general tolerance to modification and extent of such tolerance;

- specific positions and regions of sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which the retain the biological activity if the intact protein; and
- the specification provide essentially no guidance as to which of the essentially infinite possible choice is likely to be successful.

Thomas E. Creighton, in his book, "*Proteins: Structures and Molecular Properties, 1984*", (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes: 1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a Praline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "*Protein Structure: A Practical Approach, 1989; pages 184-186*" teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "*Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph)* adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Therefore, the specification fails to provide guidance regarding how to make and use polypeptides that fall within the broadly claimed genus of SEQ ID NO:11 that retain the claimed activity as well as how to make and use variants or fragments of SEQ ID NOs: 23 and 35.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting polypeptides that fall within the broadly claimed genus of variants or fragments of SEQ ID NOs: 23 and 35 having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptides that are fall within the broadly claimed

genus variants or fragments of SEQ ID NOs: 23 and 35 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

Applicants Arguments:

A) Applicant urges that claims 53 and 56 have been amended to recite that within the limit of 80% and 80% sequence identity, the claimed variant comprises the entire conserved region amino acids of SEQ ID Nos. 23 or 35, respectively. Applicant urges that the low level of variation is restricted to the V region amino acids in SEQ ID Nos. 23 and 35. Applicant urges that the specification has always disclosed that is preferred to retain conserved regions as these confer immune responses to a plurality of strains of *N. meningitides*. Applicant urges that 20% variation in the V regions corresponding to the 80% identity in claim 53, amounts to only about 8 amino acid changes. Applicant urges that 10% variation in the V regions corresponding to the 90% identity in claim 56, amounts to only about 4 amino acid changes. Applicant urges that this doe not constitute undue experimentation.

B) Applicant submits that the Examiner's comments regarding predicting the immunogenicity of proteins is purely an empirical science that requires undue experimentation is not well-founded. Applicant urges that one method of predicting protein immunogenicity is bioinformatics analysis. Applicant cites a number of references to support their position.

Examiner's Response to Applicant's Arguments:

A) It is the Examiner's position that claims 53-58 do not comply with 35 U.S.C. 112, first paragraph. Applicant has shown how to make and use SEQ ID Nos: 23 and 35 but has not shown how to make variants of the polypeptide as set forth in SEQ ID Nos:23 and 35 that possesses the recited function of eliciting an immune response in a plurality of *N. meningitides* strains Applicant has not made a correlation between structure and function. Applicant has not shown which amino acids within the amino acid sequence can be changed and the protein retains its biological function of eliciting an immune response. Applicant has not given a structure for any of the claimed variants of SEQ ID NO:23 or 35. It should be noted that above cited art references (Thomas E. Creighton and Nosoh, Y. et al) teach that changes in the structure of the amino acid sequence affect the function of any given protein. This also evidenced by Bowie et al (*Science, 1990, 257:1306-1310)* teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Further, Greenspan et al. (*Nature Biotechnology 17: 936-937, 1999)*, disclose defining epitopes is not as easy as it

seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). Based on the teachings of the prior art references, Applicant is not enabled for variants of SEQ ID Nos. 23 and 35 (amino acid sequences that are 80% or 90% identical to SEQ ID Nos. 23 or 35) because Applicant has not made a correlation between the structure and function of these claimed variants.

B) To address Applicant's comment regarding, predicting the immunogenicity of proteins, while it is true that bioinformatics is a available as a current technology as evidenced by Applicant's cited reference, however as stated above, Applicant not enable a structure for any variants of SEQ ID NO:23 or 35 which comprises the entire conserved region of SEQ ID Nos. 23 or 35 and which has the recited function of eliciting an immune response to a plurality of strains of *N. meningitidis*. As stated above, Applicant has not shown which amino acids can be changed to arrive at proteins that fall within the scope of the invention. . Applicant has not correlated a structure of the claimed variants (polypeptides with 80 or 90% identity to SEQ ID Nos: 23 or 35) with the recited function (capable of eliciting an immune response to a plurality of strains of *N. meningitides)* for the claimed genus of polypeptides encompassed by the claimed invention.. Given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a directed immune response, the specification, as filed, is not enabled for the full breath of the claimed invention.

Applicant have not met their burden under 35 U.S.C. 112, first paragraph. In view of all of the above, this rejection is maintain.

.4. The rejection under 35 U.S.C. 112, first paragraph (new matter) is maintained for 53-58 for the reasons set forth on pages 9-11, paragraph 5 of the Final Office Action. The rejection is reiterated below:

Claims 53-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.* The amendment filed August 15, 2005 introduces new matter into the claims.

35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant's amendment introduces "new matter" that is not supported by the original disclosure. The specification fails to disclose the recited claim limitation "an isolated protein the entire amino acid sequence of which has at least 80% sequence identity to the entire amino acid sequence set forth in SEQ ID NO:35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides*" or the claim limitation an isolated protein the entire amino acid sequence of which has at least 90% sequence identity to the entire amino acid sequence set forth in SEQ ID NO: 23 or SEQ ID NO:35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides".* Applicant has directed the Examiner to page 3, lines 1-6 of the instant specification. Page 3 of the specification states " proteins of the invention may therefore have one or more deletions of non-conserved amino acids compared to a corresponding wild-type NhhA polypeptide". This statement merely means that the polypeptides of the inventions are polypeptides that have sequences that are less than that of the wild-type NhhA protein. The Examiner has reviewed the instant specification and has failed to find the support for the amendment which recites the claim limitations "...at least 80% sequence identity to the entire amino acid sequence set forth in SEQ ID NO:35 wherein the isolated protein is ***not a full length NhhA polypeptide*** and is capable of eliciting an immune response to a plurality of strain of *N. meningitidis*" or the claim limitation an isolated protein the entire amino acid sequence of which has at least 90% sequence identity to the entire amino acid sequence set forth in SEQ ID NO: 23 or SEQ ID NO:35 wherein the isolated protein is ***not a full length NhhA polypeptide*** and is capable of eliciting an

immune response to a plurality of strain of *N. meningitides".* Applicant is required to cancel the new matter in the reply to this Office Action.

Applicant's Arguments

Applicant urges that the recitation "is not a full length NhhA polypeptide" has been replaced in the claims by the recitation "is not a wild type NhhA polypeptide" which is fully support by the specification.

Examiner's Response to Applicant's Arguments

Although Applicant has amended the claims to included the phrase is not a wild type NhhA polypeptide" the new matter rejection is maintained for the following reasons:

The claims require that the isolated proteins have:

a) 80% or 90% to SEQ IN Nos.23 or 35,

b) comprise the entire conserved region of SEQ ID NO:23 or 35,

c) is not a wild type NhhA polypeptide and

d) is capable of eliciting an immune response in a plurality o strains of *N. meningitidis.*

The instant specification does not teach isolated proteins that are 80% or 90% of SEQ ID Nos.23 and 35, comprise the entire conserved region of SEQ ID Nos,23 and 35, which are not the wild-type NhhA polypeptide and are capable of eliciting an immune response to a plurality of strain of *N. meningitides.*

The instant specification teaches that the isolated proteins of the invention comprise one or more constant regions (c regions) of an NhhA polypeptide (page 3). The specification teach fragments of the isolated proteins that have less than 100%

identity (20%, 50%, 80% or 90% identity) to the isolated proteins of the invention (page 13). The specification teach polypeptide homologs that have 70% or 80% or 90% identity to protein of the invention. It should be noted that the fragments and homologs disclosed according to pages 13 and 15 of the specification are not required to comprise the entire conserved region of SEQ ID Nos. 23 or 35 nor are they required to have the recited biological function of eliciting an immune response in a plurality of strains of *N. meningitidis*..

In view of all of the above, this new matter rejection is maintained.

5. The rejection under 35 U.S.C. 112, first paragraph (written description) is maintained for 53-58 for the reasons set forth on pages 11-13, paragraph 6 of the Final Office Action.

The rejection is reiterated below:

Claims 53-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as an isolated protein the entire amino acid sequence of which has at least 80% sequence identity to the entire amino acid sequence set forth in SEQ ID NO:35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides"* or the claim limitation an isolated protein the entire amino acid sequence of which has at least 90% sequence identity to the entire amino acid sequence set forth in SEQ ID NO: 23 or SEQ ID NO:35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides"*.

The specification teaches proteins of the invention may therefore have one or more deletions of non-conserved amino acids compared to a corresponding wild-type NhhA polypeptide (page 3). The specification also teaches that polypeptides homologs share at least 70%, preferably 80% and more preferably at least 90% identity with the

amino acid sequences of modified NhhA polypeptides of the invention (page 15). However, the instant specification has failed to teach or disclose isolates proteins that have at least 80% identity to SEQ NO:35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strains *N. meningitides"* or isolated proteins that have at least 90% identity to SEQ ID Nos: 23 and 35 wherein the isolated protein is not a full length NhhA polypeptide and is capable of eliciting an immune response to a plurality of strains *N. meningitides"*.

Thus, the instant specification lacks written description for the claimed invention.

Therefore, claimed invention fails to meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, the instant specification does not provide written description for the full breadth of the claim. Thus the broadly claimed invention does not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant's Arguments

Applicant urges that the recitation "is not a full length NhhA polypeptide" has been replaced in the claims by the recitation "is not a wild type NhhA polypeptide" which is fully supported by the specification.

Examiner's Response to Applicant's Arguments

Although Applicant has amended the claims to included the phrase is not a wild type NhhA polypeptide" the new matter rejection is maintained for the following reasons:

The claims require that the isolated proteins have:

a) 80% or 90% to SEQ IN Nos.23 or 35,

b) comprise the entire conserved region of SEQ ID NO:23 or 35,

c) is not a wild type NhhA polypeptide and

d) is capable of eliciting an immune response in a plurality o strains of *N. meningitidis*.

The instant specification does not teach isolated proteins that are 80% or 90% of SEQ ID Nos.23 and 35 which comprise the entire conserved region of SEQ ID Nos,23 and 35, which are not the wild-type NhhA polypeptide and are capable of eliciting an immune response in a plurality o strains of *N. meningitidis*.

The instant specification teaches that the isolated proteins of the invention comprise one or more constant regions (c regions) of an NhhA polypeptide (page 3). The specification teach fragments of the isolated proteins that have less than 100% identity (20%, 50%, 80% or 90% identity) to the isolated proteins of the invention (page 13). The specification teach polypeptide homologs that have 70% or 80% or 90%

identity to protein of the invention. It should be noted that the fragments and homologs disclosed in the instant according to pages 13 and 15 of the specification are not required to comprise the entire conserved region of SEQ ID Nos. 23 or 35 nor are they required to have the recited biological function of eliciting an immune response in a plurality o strains of *N. meningitidis.*

The instant specification does not provide written description for the full breadth of the claim (e.g. isolated proteins that have 80% or 905% identity to SEQ ID 23 or 35, which comprises the entire conserved region amino acids of SEQ ID Nos, 23 or 35, respectively wherein the isolated protein is not a wild-type NhhA polypeptide and is capable of eliciting an immune response to a plurality of strains of *N. meningitidis*). Thus, the broadly claimed invention does not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

In view of all of the above, this new matter rejection is maintained.

Status of Claims

6. Claims 33-34 and 49-58 appear to be free of the cited prior art. The closet prior art, Peak et al *(WO 99/31132 published June 24, 1999)* or Peak et al *(U.S. Patent No. 6,197, 312 B1 published March 2001)* or Masignani et al *(WO 99/36544 published July 22, 1999)* do not teach or disclose an isolated protein having the amino acid sequence

SEQ ID NO:23 or a mature processed form of the isolated protein having the amino acid sequence of SEQ ID NO:35. Peak et al *WO 99/31132 published June 24, 1999)* or Peak et al *(U.S. Patent No. 6,197, 312 B1 published March 200)1* nor Masignani et al teach polypeptides that have at least 80% sequence identity to the entire amino acid sequence set forth in SEQ ID NO:35 wherein the isolated protein is not a wild-type NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides*" or the claim limitation an isolated protein the entire amino acid sequence of which has at least 90% sequence identity to the entire amino acid sequence set forth in SEQ ID NO: 23 or SEQ ID NO:35 wherein the isolated protein is not a wild-type NhhA polypeptide and is capable of eliciting an immune response to a plurality of strain of *N. meningitides".* The prior art also do not teach compositions comprising these polypeptides.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vanessa L. Ford
Biotechnology Patent Examiner
August 15, 2007

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER